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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/655,815	09/06/2000	Robert Lanza	P 0275705 23523-0162	8460

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EXAMINER	
TON, THAIAN N	
ART UNIT	**PAPER NUMBER**
1632	16

DATE MAILED: 12/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/655,815	LANZA ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,11-19,29-32 and 34-55* is/are pending in the application.

4a) Of the above claim(s) *15-19,29-32,34-37 and 49-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,11-14 and 38-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicants' Amendment, filed 9/10/02, Paper No. 14, has been entered. Claims 1, 38 and 48 have been amended. Claims 8-10, 20-28 and 33 have been cancelled.

Claims 1-7, 11-19, 29-32, 34-55 are pending. Claims 1-7, 11-14, 38-48 are under current examination.

Any rejection made of record in the prior Office action, mailed 4/10/02, Paper No. 10, and not made of record in the instant Office action, has been withdrawn in view of Applicants' arguments and/or amendments to the claims.

Specification

The substitute specification filed 9/10/02 has not been entered because it does not conform to 37 CFR 1.125(b) because the following has not been provided:

> A marked-up copy showing the amendments to be made via the substitute specification relative to the specification at the time the substitute specification is filed.

Correction of Inventorship

In view of the papers filed10/24/02, Paper No. 15, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been

corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by addition of Jose Cibelli.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected.

Claim Rejections - 35 USC § 101

The prior rejection of claims 38, 41-43 is withdrawn in view of Applicants' amendment(s) to the claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7, 11-14 and 38-48 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over

claims 1-14 and 38-48 of copending Application No. 09/797,684. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to methods of testing immune compatibility of cloned cells or tissues in an animal model by producing en embryo by nuclear transfer, injecting the embryo, disc or stem cell isolated from the embryo into a donor animal and examining the injection site for teratoma formation and signs of rejection of the injected cells, the claims are further directed to a non-human, non-immune-compromised animal containing at least one teratoma produced from a cloned cell, and teratomas isolated from the non-human animal. The '684 claims are directed to methods of methods of testing immune compatibility of cloned cells or tissues from an animal model comprising generating an embryo via nuclear transfer, injecting the embryo, disc, or stem cell isolated from the embryo into a donor animal, and examining the injection site for teratoma formation, a non-human animal containing at least one teratoma produced from a cloned cell, and teratomas isolated from the non-human animal. Both sets of claims are directed to methods of testing immune compatibility of cloned cells or tissues from an animal model, non-human animals containing at least one teratoma, and teratomas isolated from the non-human animal. The instant claims differ from the '684 claims in that they are broader in scope, for example, claim 2 of the instant application recites that the cell is transfected with a heterologous gene prior to nuclear transfer, and claims 8-10 of the '684 application specifically recite particular proteins.

Furthermore, claim 38 of the instant application recites a non-human, non-immune-compromise animal containing a teratoma, which is broader in scope the than non-human animal containing a teratoma, wherein the animal is a mammal selected from the group consisting of a non-human primate, an ungulate and dog, as claimed in claim 38 of the '684 application. However, all of the instant claims are made obvious by the '684 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of claims 1-7 and 11-14 under 35 U.S.C. 112, first paragraph, is maintained, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record advanced on pages 5-12 of the prior Office action.

Applicants argue that claim 1 has been amended to recite enucleating an oocyte and using as a recipient cell in nuclear transfer, although Applicants traverse this requirement to require fusing of the donor cell to the recipient cell, and

activating the resulting nuclear transfer unit to generate the embryo. Applicants argue that while nuclear transfer cloning is routinely performed by a method that comprises fusing the donor cell to the recipient cell, those in the art recognize that it can also be performed successfully by removing the nucleus of the donor cell, injecting the donor nucleus into the recipient cell, a technique that does not require the step of fusing the donor and recipient cell membrane. Furthermore, Applicants argue that those skilled in the art will recognize that the step of activation of a nuclear transfer unit to generate an embryo can be carried out by a variety of means, including passively incubating the nuclear transfer unit so that it activates spontaneously. Applicants argue that it would be improper for the pending claims to be limited to a method that usese one particular method for producing a nuclear transfer embryo out of the various combinations of methods for making nuclear transfer embryos that are known in the art. [See p. 7, 2nd ¶ of the Response].

Applicants' arguments and amendments have been considered, however, they are not found fully persuasive. The Examiner agrees that although fusion of the donor cell to the recipient cell is not the only method that can be used to generate a nuclear transfer embryo, it is reiterated that activation of the resulting nuclear transfer unit must take place in order to effect further development. For example, Dinnyés *et al.* [**Cloning & Stem Cells**, 4:81-90, 2002] report on the state of the art of somatic cell nuclear transfer state that, "NT is a complex procedure and each step effects the overall efficiency. The unpredictability of the technology due to biological

variation of the recipient oocytes and the donor cells is difficult to control. Therefore, standardization of the steps is important in order to obtain consistent results." [See p. 83, 1st column, 2nd full paragraph]. With particular regard to the importance of the activation of oocytes, Dinnyés *et al.* state that, "In NT, the lack of sperm-induced fertilization steps necessitate the application of an artificial activation in order to trigger further development." [See p. 83, 2nd column, last paragraph]. Thus, it is maintained that the claimed methods of testing the immune compatibility, which require a nuclear transfer unit and further generation of an embryo, would not be predicted to result in a successful nuclear transfer, as the claims do not provide an activation step.

It is further noted that the claimed invention is directed to methods for testing immune compatibility of cloned cells or tissues in an animal model. The specification broadly discusses methods of testing immune compatibility (see p. 7, lines 1-9, for example). The specification discusses a method to test immune compatibility in nuclear transfer-generated cells in cattle (see Example 1). However, the specification does not provide sufficient teaching or guidance to show how the cattle carrying the teratomas would be tested for immune compatibility. The specification broadly discusses that the teratomas would be, "removed for histological analysis" (see p. 17, lines 26-27), but there is no particular guidance or working examples provided by the specification to show how these tissues would be analyzed and tested for immune compatibility. The specification must teach those

skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. Although the specification provides a hypothesis (the specification teaches that it is expected that the "same animal" stem cells would survive in the recipient (donor of the nucleus) animal in contrast to "different animal" stem cells, see p. 18, lines 6-11), the specification does not provide particular teaching or guidance to show how the claimed method would be used to test immune compatibility, and as such, it is reiterated that undue experimentation would have been required to implement the claimed methods.

Accordingly, in view of the specification's lack of guidance or working examples provided by the specification for methods of testing immune compatibility, it would have required undue experimentation for one skilled in the art to carry out the claimed methods.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The prior rejection of claim 38 is withdrawn in view of Applicants' amendment to the claim, in particular, the recitation of non-human, non-immune compromised. The prior rejection of claims 44-47 are rejected under 35

U.S.C. 102(b) as being anticipated by Anderson *et al.* (**Ani Reprod Sci**, Vol. 45, 1996, pp. 231-240) is maintained for reasons of record advanced on pages 14-16 of the prior Office action.

Applicants argue that claim 38, as amended, recites a non-human, non-immune compromised animal containing at least one teratoma produced from a cloned cell, and that Anderson does not disclose transplanting cloned pluripotent embryonic cells into a non-immune-compromised animals to form a teratoma [see p. 9, 1st ¶ of the Response].

Applicants' arguments have been carefully considered, however, they are not found fully persuasive. It is noted that the claims are product-by-process claims [see p. 14 of the prior Office action]. As such, the claims are properly interpreted as a teratoma, wherein the teratoma contains cells from all three germ layers, and the teratoma is derived from a cloned ungulate cell.

Anderson *et al.* teach the implantatation of inner cell masses and embryonic discs from bovine and porcine blastocysts under the kidney capsule of nude mice (see *Abstract*). Specifically, Anderson *et al.* teach that athymic BALB/C mice were used as hosts for embryonic grafts. The mice were implanted with two to four inner cell masses, embryonic discs, egg cylinders or intact Day 8 *in vitro* derived bovine blastocysts which were deposited under the kidney capsule (see p. 233, 2.2). Anderson *et al.* teach that the mice were killed by cervical dislocation 8 weeks after transplantation and the tumors were excised from the kidney. These tumors were

classified as benign teratomas, or malignant teratocarinomas. Selected tumors were stained immunohistochemically for the presence of various markers (see p. 233, 2.3). Anderson *et al.* teach that the representation of cell types was ectodermal, mesodermal and endodermal origins in the bovine and porcine tumors and was somewhat more restricted than from murine embryonic tumors (see *Abstract*).

Accordingly, Anderson *et al.* anticipate claims 44-47.

Amended claims 38-40 and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Hibbs *et al.* [**Am. J. Vet. Res.**, 29:1891-1894, 1968].

Note that instant claims recite that the teratoma is "produced from a cloned cell". As such, the limitation of the teratoma is properly interpreted as a product-by-process, see MPEP §2113, "Even though product-by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." Accordingly, the claims are properly interpreted as a non-human, non-immune compromised animal that contains at least one teratoma.

Hibbs *et al.* teach heifers that are found to have teratomas [see *Summary*, p. 1891].

Accordingly, Hibbs anticipate the claimed invention.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thaian N. Ton whose telephone number is (703) 305-1019. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the examiner be unavailable, inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to Tiffiany Tabb, Patent Analyst, at (703) 605-1238. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Deborah Crouch

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